

# BMJ Open Prediction and prognostication of neurological deterioration in patients with acute ICH: a hospital-based cohort study

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## ABSTRACT

**Objective:** Patients with intracerebral haemorrhage (ICH) are at high risk of neurological deterioration (ND). We aimed at establishing predictors of early ND (END) as well as late ND (LND) and at exploring the impact of neurological stability during the first week on long-term prognosis.

**Design:** We conducted this study as a retrospective cohort study. ND was evaluated based on the consciousness and severity of neurological symptoms. ND during the first 24 h after admission was defined as early ND and from 24 h to 7 days as LND. Patients were followed up until February 2015.

**Participants:** We included 300 patients with acute ICH ( $\leq 4.5$  h from symptom onset) who were admitted to our institution from March 2009 to January 2015.

**Setting:** Section of Acute Neurology, Department of Neurology, Bispebjerg Hospital is a specialised referral centre receiving patients with acute stroke from the entire capital region of Denmark.

**Results:** We found that a spot sign on CT angiography (OR 10.7 CI 4.79 to 24.3) and extensive degree of intraventricular haemorrhage (IVH) (OR 8.73 CI 2.87 to 26.5) were independent predictors of END, whereas a degree of comorbidity (Charlton Index), admission stroke severity and degree of IVH predicted LND. On follow-up imaging, haematoma expansion was independently associated with END (OR 6.1 CI 2.2 to 17.3), and expansion of IVH was independently associated with both END (OR 1.7 CI 1.2 to 2.3 per point increase) and LND (OR 2.3 CI 1.3 to 4.2 per point increase). ND during the first week was associated with a 1-year mortality of 60.5%, compared with 9.2% among the patients who remained stable.

**Conclusions:** These results suggest that stability during the first week entails an optimistic prognosis. A relatively easy and effective risk stratification of END and LND is possible on admission based on the spot sign, IVH and clinical parameters.

## INTRODUCTION

Neurological deterioration (ND) in patients with intracerebral haemorrhage (ICH) is

## Strengths and limitations of this study

- The main strengths of this study are its fairly large sample size of patients with acute intracerebral haemorrhage (ICH) included consequently without selection.
- The large proportion of the patients worked up with CT angiography in the acute setting allowing us to include the spot sign as a prognostic marker; and the detailed follow-up regarding outcome allowing very few people to be lost to follow-up.
- The major limitation of this study is the incomplete use of follow-up imaging 24 h after stroke onset. Both patients with mild ICH and those with devastating strokes might be less likely to receive follow-up imaging. We chose to include all patients to keep the study population as unselected as possible.

common, as approximately 25% of patients deteriorate within the first 2 days following admission.<sup>1–5</sup> However, even though the incidence of early ND (END) is well described, easy-to-use predictors allowing a better ultra-early risk stratification in terms of identifying unstable patients are not well established. New imaging concepts such as the CT angiography (CTA)-based spot sign, which have been proved to predict haematoma expansion, are most likely a powerful tool in the acute risk stratification of patients with ICH. Further, little is known about late ND (LND), even though the existence of LND is well established among clinicians.<sup>4 6</sup> Evidence indicates that structural damage as well as secondary space-occupying lesions in the brain occurs predominantly during the very first days of illness<sup>7–12</sup> (provoking END and LND). Assuming minimisation of complications by means of adequate stroke unit care (including aspiration pneumonia,

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venous embolisms, urinary tract infections, etc),<sup>13 14</sup> we propose that clinical neurological stability during the initial week after stroke onset will translate into an overall stability of the patient and hence a lower risk of long-term morbidity and mortality. Therefore, the aim of the present study was to establish predictors of END and LND present on admission as well as the significance of the acute phase of illness on the long-term prognosis.

## METHOD

The Department of Neurology, Bispebjerg Hospital maintains a database with ongoing registration of consecutive patients with primary ICH admitted to the acute stroke unit within 4.5 h after symptom onset. This study was conducted as a retrospectively planned analysis based on this cohort including patients admitted to our acute stroke unit from March 2009 to January 2015. The number of arriving patients determined the sample size. Patients were excluded if deeply comatose on admission (Glasgow Coma Scale (GCS) <5) or if later diagnostic workup revealed an underlying cause of the haemorrhage (final diagnosis not primary ICH). On arrival, patients underwent a standardised workup including non-contrast CT (NCCT), and a National Institute of Health Stroke Scale (NIHSS) score was obtained. Patients further underwent acute CTA if no contraindication to the procedure (allergy or significant kidney failure) was present. Patients with ICH were treated in accordance with guidelines from the European Stroke Organisation.<sup>15 16</sup> They were continuously monitored, and vital values as well as GCS and neurological symptoms (stroke in progression (SIP) score) were recorded at least every hour within the first 24 h by the nursing staff. The SIP score is a shortened version of the Scandinavian Stroke Scale and is used for purposes of monitoring patients with acute stroke<sup>17</sup> (see online supplementary materials). Follow-up imaging was scheduled to be performed approximately 24 h after admission or earlier in case of ND. When patients were assumed to be stable, they were transferred to rehabilitation in local hospital stroke units based on the abode of the patient. Local stroke units are monitored on quality, and all comply with the national standards regarding stroke unit care. A more detailed description of treatment procedures is presented in the online supplementary materials.

## Neurological deterioration

ND was defined as a decrease of  $\geq 2$  GCS points<sup>18</sup> or  $\geq 4$  SIP score points, lasting longer than 8 h, requiring surgical intervention, or resulting in death. The cut point of 4 SIP score points was made based on the widely accepted 4 point NIHSS cut point<sup>3 19</sup> when defining ND and the conversion formula between the Scandinavian Stroke Scale and NIHSS.<sup>20</sup> END was defined as occurring within the first 24 h after admission,<sup>3 18 19 21</sup> with

the admission value of GCS and SIP score as the baseline reference. The presence of END was confirmed based on the documented GCS and SIP score values along with medical chart descriptions. LND was defined as occurring later than 24 h after hospital admission, but within the first 7 days.<sup>6</sup> LND was confirmed based on a review of all medical chart data from days 1 to 7. Documented progression in the patient's condition equal to  $\geq 2$  GCS points or  $\geq 4$  SIP score points with the GCS and SIP score values at 24 h after admission as reference and with no other obvious non-neurological cause such as infection or pulmonary embolism was defined as LND. Only patients who were stable during the first 24 h and non-surgically treated were assessed for LND. If patients were discharged within the first week after symptom onset, they were presumed to be continuously stable. A consultant neurologist (HC) with extensive experience in stroke neurology assessed the medical charts to confirm LND.

## Definitions of patient characteristics and comorbidity

Detailed descriptions on the definition of patient characteristics are presented in online supplementary materials. Disability prior to stroke onset was graded using the modified Rankin Scale (mRS), and degree of comorbidity was graded using the Charlson Comorbidity Index.<sup>22</sup>

## CT and CTA imaging and analysis

A senior consultant neuroradiologist (AFC) and two board-certified radiologists (IH and EK) reviewed all imaging in a systematic manner blinded to clinical data. We defined the presence of the spot sign as one or more 1–2 mm foci of enhancement within the haematoma on CTA source images<sup>23</sup> (imaging protocol details are presented in the online supplementary materials). Haematoma volumes were calculated using the ABC/2-method.<sup>24</sup> Significant haematoma expansion was defined as an increase in haematoma volume of  $\geq 12.5$  mL between admission and follow-up NCCT. The volume and extent of the intraventricular haemorrhage (IVH) were graded using the semiquantitative Graeb Score.<sup>25</sup> Subarachnoid extension of the haemorrhage (SAH) was defined as clearly visible blood in the subarachnoid space. Delayed IVH or SAH was defined as IVH or SAH on follow-up imaging, not present on admission imaging. Midline shift was measured as the distance from the septum pellucidum between the frontal horns of the lateral ventricles to a line connecting the anterior and posterior insertions of the falx cerebri on a CT slice containing the third ventricle.<sup>8</sup> Hydrocephalus was defined as marked dilation of one or more of the ventricles.

## Follow-up

Patients were followed through the national electronic chart system. Outcome at 90 days was assessed based on records from the outpatient clinic or occupational

therapy. Good outcome was defined as the ability to walk independently (mRS  $\leq 3$ ). Mortality of the patients was collected during the first year after the admission date or until 20 February 2015. Patients who were not Danish citizens were censored the day they left the country.

## Statistics

We compared normally distributed data using Student *t* test, non-normally distributed data and ordinal scale data using the Mann-Whitney U-test and categorical data using the  $\chi^2$  test. We designed prediction models for END and LND using logistic regression. Baseline data that were significantly different between the two groups ( $p < 0.05$ ) were added into the models and excluded in a backward stepwise manner. In the models, we included NIHSS as the estimator of admission neurological status due to its widespread international use. GCS or SIP score was not additionally included due to collinearity concerns. On the basis of data from the follow-up imaging, we constructed two additional logistic models for END and LND. Radiological variables significantly different between the groups were included in the models. If measures of enlargement of radiological variables (eg, absolute haematoma expansion) were used in the models, we also adjusted for baseline variables (eg, admission haematoma volume). Non-adjusted survival analysis during the first year after admission was undertaken using Kaplan-Meier curves stratified for ND during the first 7 days. ND was used as a collective term for END and LND. The independent effect of ND on 90 days functional outcome and long-term mortality was assessed using logistic regression (good 90-day outcome) and Cox Proportional Hazard Model (long-term mortality). We included age and gender and degree of comorbidity (Charlson Score), factors known to be associated with ICH outcome,<sup>26</sup> and surgical procedures in

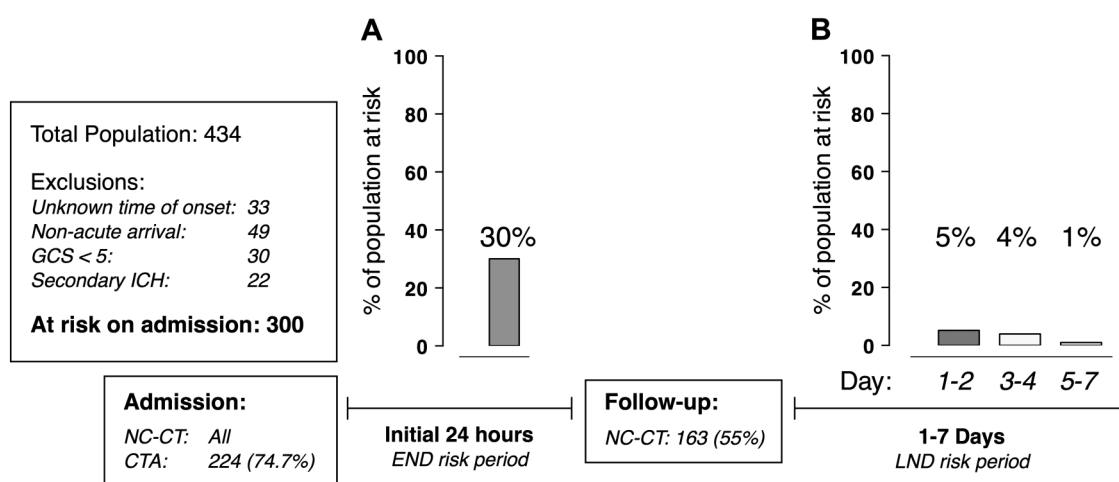
the models. ND was entered as a time-dependent variable to avoid the immortal time bias. The  $p < 0.05$  was considered to be significant. Statistical analyses were performed in SPSS V.20 statistical software (IBM Corp, Armonk, New York, USA).

## RESULTS

We included 300 patients with acute primary ICH in the cohort (figure 1). All patients received admission NCCT (224 (74.7%) underwent acute CTA) with a median (IQR) delay from symptom onset of 103.0 min (76.3–143.0). At least one follow-up NCCT was performed in 163 (54.3%) patients with a median (IQR) delay from admission CT of 19 (10–25) h.<sup>10–25</sup> One patient underwent external ventricular drain installation immediately after admission without indication of END. This patient was excluded from further analysis. Five patients underwent surgical evacuation of the haematoma, and three underwent placement of external ventricular drainage without previous ND. These patients were excluded from analysis at the time they underwent surgery.

### Early neurological deterioration

Of the 299 patients, 89 (29.7%) fulfilled the criteria of END (figure 1). Among admission characteristics (see online supplementary table S1), END was most notably associated with higher NIHSS (17 (11–22) vs 10 (5–16),  $p < 0.0001$ ), lower GCS (12 (10–14) vs 15 (13–15),  $p < 0.0001$ ), higher admission haematoma volume (45.1 mL (18.0–88.9) vs 10.1 mL (3.5–24.0),  $p < 0.0001$ ), and larger degree of midline shift (2.0 mm (0.0–7.0) vs 0.0 mm (0.0–0.0),  $p < 0.0001$ ), in addition to a higher frequency of IVH (51.7% vs 24.8%,  $p < 0.0001$ ), SAH (37.1% vs 16.7%,  $p < 0.0001$ ) and spot sign (73.4% vs 18.1%,  $p < 0.0001$ ). END was significantly associated with prestroke oral



**Figure 1** Study outline and prevalence of neurological deterioration during the first week. Panel (A) describes the incidence of END during the first 24 h, and panel (B) describes the incidence of LND during the following 6 days (CTA, CT angiography; END, early neurological deterioration; GCS, Glasgow Coma Scale; ICH, intracerebral haemorrhage; LND, late neurological deterioration; NC-CT, non-contrast CT).



anticoagulation treatment (22.7% vs 9.5%,  $p=0.005$ ) but not treatment with platelet inhibitors. Duration of time from admission to reversal of anticoagulation treatment commenced was similar for stable patients and patients suffering END. Of the patients with END, 20 (22.5%) required intubation with a median (IQR) time from symptom onset of 3.0 h (2.0–4.0). Eleven (12.4%) patients with END underwent placement of an external ventricular drain with a median (IQR) time to drain placement of 6.0 h (4.0–17.0). Seventeen (19.1%) of the patients with END underwent surgical removal of the ICH—all with the indication of pending herniation. Of the patients with END, 34 (38.2%) had a do-not-resuscitate (DNR) order placed on their charts within the first 24 h after admission compared with only 11 (5.2%) of the stable patients ( $p<0.0001$ ). In multivariate analysis among the 224 patients with CTA on admission (table 1), the most notable predictors of END were the spot sign, anticoagulation treatment, and extensive IVH. This model provided excellent discriminative capability towards END (C-statistics=0.87, CI 0.82 to 0.92). If CTA data were not considered ( $n=299$ ), the significant predictors of END were oral anticoagulation treatment, extensive IVH, and more severe stroke symptoms (NIHSS) on admission. Patients with haematoma volumes below 10 mL were at low risk. This model also provided a good discriminative capability towards END (C-statistics=0.82, CI 0.77 to 0.88). On a follow-up scan, significant haematoma expansion and IVH expansion were independently associated with END (table 2). Of the 36 patients with END who were alive and non-surgically treated after the initial 24 h, 19 (52.8%) deteriorated further within the following 6 days.

### Late neurological deterioration

After the first 24 h, 204 patients remained stable and non-surgically treated. During the next 6 days, 20 (9.6%) patients who were stable during the initial 24 h suffered LND (figure 1). Patients with LND (see online supplementary table S1) most notably had a significantly higher degree of comorbidity (median Charlson Score 1 (0.5–2) vs 0 (0–1),  $p=0.003$ ), higher admission NIHSS (15 (13–20) vs 9 (5–15),  $p<0.0001$ ), lower admission GCS (13 (11–14) vs 15 (13–15),  $p=0.002$ ), higher admission volume (28.5 mL (12.5–44.1) vs 9.2 mL (3.0–21.1),  $p=0.002$ ), and higher frequency of IVH (60.0% vs 19.6%,  $p<0.0001$ ) compared with patients who remained stable. In multivariate analysis, the significant predictors present on admission of LND were higher degree of comorbidity (Charlson Score), more extensive IVH, and higher admission NIHSS. This model provided excellent discriminative capability towards LND (C-statistics=0.86, CI 0.76 to 0.95). On a follow-up scan, final extension of the IVH was found to be associated with LND, and expansion of the IVH was an independent predictor when adjusted for extension of baseline IVH (table 2). Of the patients with LND, 12 (60.0%) had a DNR order placed on their charts with a median (IQR) delay of 3 days (0–4) after admission. Of the patients who

**Table 1** Independent predictors of END and LND

	OR	95% CI	p Value
END—patients with CTA on admission (n=224)			
Anticoagulation treatment	3.41	1.19 to 9.80	0.023
Admission Graeb Score			
0 points	1.00	—	—
1–5 points	2.02	0.76 to 5.40	0.161
6–12 points	8.73	2.87 to 26.5	<0.001
Admission haematoma volume			
>60 mL	1.00	—	—
10–59.9 mL	0.43	0.18 to 1.06	0.066
<10 mL	0.27	0.09 to 0.82	0.021
Spot sign	10.7	4.79 to 24.3	<0.001
END—all patients (n=299)			
Anticoagulation treatment	3.87	1.65 to 9.11	0.002
Admission Graeb Score			
0 points	1.00	—	—
1–5 points	1.59	0.73 to 3.46	0.241
6–12 points	4.63	1.79 to 12.0	0.002
Admission SAH	2.24	1.03 to 4.87	0.042
Admission haematoma volume			
>60 mL	1.00	—	—
10–59.9 mL	0.44	0.20 to 0.95	0.037
<10 mL	0.20	0.07 to 0.56	0.002
Admission NIHSS (per point)	1.08	1.03 to 1.14	0.002
LND—all patients at risk at day 1 (n=204)			
Charlson Score (per point)	1.74	1.18 to 2.55	0.005
Haematoma location			
Lobar	1.00	—	—
Basal ganglia	0.17	0.05 to 0.59	0.005
Posterior fossa	0.22	0.02 to 3.14	0.263
Admission Graeb Score			
0 points	1	—	—
1–5 points	4.81	1.42 to 16.3	0.012
6–12 points	22.2	3.66 to 134.8	0.001
Admission NIHSS (per point)	1.13	1.03 to 1.23	0.014

Variables offered to both END models were anticoagulation treatment, admission Graeb Score, SAH on admission, serum glucose level, admission midline shift, admission haematoma volume, and admission NIHSS value (the spot sign presents only the first model). Variables offered to the LND model were Charlson Score, admission NIHSS, admission haematoma volume, admission Graeb Score, and admission midline shift. CTA, CT angiography; END, early neurological deterioration; LND, late neurological deterioration; NIHSS, National Institute of Health Stroke Scale; SAH, subarachnoid hemorrhage.

remained stable during the entire first week, only 7 (3.7%) had a DNR order placed on their charts with a median delay (IQR) from admission of 0 days (0–0).

### Outcome

After 90 days, 122 (72.2%) of the surviving patients, who remained stable during the first 7 days, were able to walk independently compared with 9 (20.5%) of the patients who suffered ND ( $p<0.0001$ ). Adjusted for significant prognostic factors (age, admission NIHSS, IVH, admission haemorrhage volume, and haematoma location),

**Table 2** Follow-up imaging characteristics

	Early neurological deterioration		Late neurological deterioration	
	Crude OR	Adjusted OR*	Crude OR	Adjusted OR†
Significant haematoma expansion, >12.5 mL	15.0 (6.3 to 35.5)	6.1 (2.2 to 17.3)	2.0 (0.4 to 10.5)	NI
Follow-up Graeb Score, per point	1.3 (1.2 to 1.5)	NI	1.5 (1.2 to 1.9)	NI
Delayed IVH	10.3 (3.2 to 33.3)	NI	2.6 (0.2 to 26.6)	NI
IVH expansion, per Graeb point	11.0 (4.4 to 27.2)	1.7 (1.2 to 2.3)	5.5 (1.1 to 26.3)	2.3 (1.3 to 4.2)
SAH on the follow-up scan	3.4 (1.6 to 7.3)	2.8 (0.8 to 9.3)	2.6 (0.7 to 9.5)	NI
Delayed SAH	3.4 (0.6 to 21.3)	NI	NA	NA
Hydrocephalus	5.3 (1.7 to 16.3)	1.4 (0.3 to 6.6)	2.6 (0.2 to 26.6)	NI
Midline shift, per mm	1.3 (1.1 to 1.4)	1.1 (0.9 to 1.3)	1.2 (0.9 to 1.4)	NI

\*We adjusted for admission haematoma volume and admission Graeb Score.

†We adjusted for admission Graeb Score.

IVH, intraventricular haemorrhage; NA, not assessed due to incomplete representation; NI, not included in the model due to insignificance or representation by other values (collinearity); SAH, subarachnoid hemorrhage.

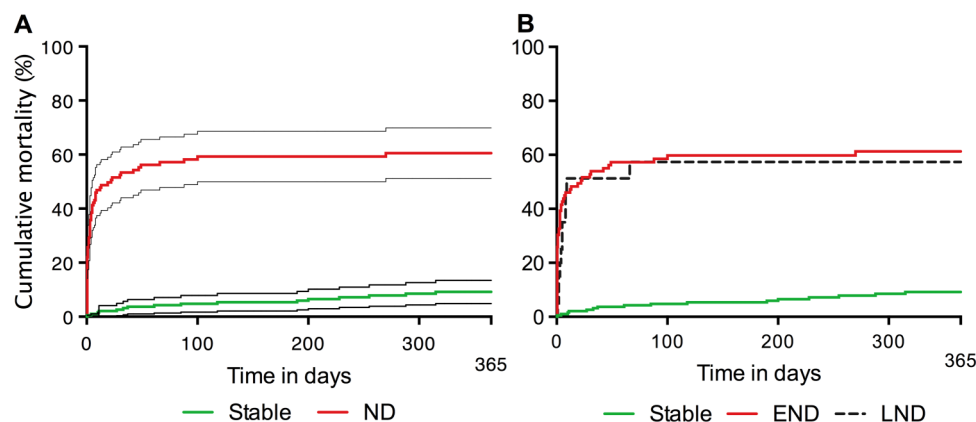
comorbidity (Charlson Score) and surgical procedures (surgical evacuation and instalment of external ventricular drainage), ND was an important inverse predictor of good outcome (OR 0.11 CI 0.04 to 0.32) (see online supplementary table S2).

One year after admission, 60.5% (CI 51.2% to 69.8%) of the patients who suffered ND during the first 7 days after admission had died (figure 2A). In comparison, only 9.2% (CI 4.9% to 13.5%) of the patients who remained stable during the first 7 days had died ( $p<0.0001$ ). The median survival of the patients who suffered ND was 20 days. Patients with END and LND suffered comparable mortality during the first year (figure 2B). When the same significant prognostic factors as above were controlled for, ND was established as an important predictor of long-term mortality (HR 6.99 CI 3.54 to 13.8) (see online supplementary table S2). Other independent predictors of mortality during the first year were age, Charlson Score, admission NIHSS, posterior fossa location, and admission haematoma volume. We only included surgical treatment of patients with pending herniation, and it appeared to affect survival; however, it was not a predictor of good functional outcome.

## DISCUSSION

Patients who remained stable during the first week after stroke onset were most likely to survive the first year. Haematoma expansion is a key driving force behind END, and factors that mark the patients as unstable within the first day were essentially risk factors of haematoma expansion—spot sign, larger haematomas and anticoagulation treatment. Patients with smaller haematomas seemed to be protected from END. In addition, extensive haemorrhage into the ventricles of the brain marked the patients as unstable during the entire first week.

This study has several strengths. We believe that the generalisability of the data is high, as this study is based on consecutive patients with as little selection as possible as they were admitted based on the catchment area. Patients are admitted fast track with early symptoms of stroke, independent of, for example, age or stroke severity. The electronic follow-up of patients allowed this to be almost complete, and only very few (all foreign citizens) were lost to follow-up. The large majority of patients in this study underwent acute CTA enabling us to investigate the spot sign as a risk factor of ND.



**Figure 2** Survival curves displaying mortality during the first year. Panel (A) shows the cumulative mortality ( $\pm 95\%$  CI) of stable patients and patients with neurological deterioration (ND) during the first week. Panel (B) shows the cumulative mortality separated into patients with early ND (END), late ND (LND), and stable neurological status during the first week.

A weakness is the incomplete use of follow-up imaging, which could impose concerns of selection bias in the analysis of the follow-up images; however, the frequency of follow-up imaging was distributed equally among stable patients and patients suffering END or LND. It remains likely that the moribund patients, who might have concealed a large portion of haematoma expansion or IVH, as well as patients with mild symptoms were the groups most likely to be excluded from the follow-up scan. Another weakness is the way in which LND was assessed. We did not possess consecutive GCS and SIP score data further than the first day in most patients, and we thus needed to rely on medical chart data with documentation of GCS and the physicians' description of LND. However, physicians in Denmark are obligated to keep rigorous medical records, and because of this we believe that even though it could provide information bias, it was an acceptable way to assess LND.

Our data are consistent with other studies documenting a substantial risk of ND during the first 24–48 h. The relatively high fraction of patients undergoing END in our study is most likely due to the exclusion of comatose and surgically treated patients<sup>2–4</sup> from other studies on END. LND is relatively poorly described in the literature. Mayer *et al*<sup>4</sup> documented an incidence of LND relatively similar to ours. Sun *et al*<sup>6</sup> found a higher incidence of LND, but did not exclude patients suffering END. We demonstrated that patients who already have suffered END will be at high risk of continuing their trajectory of deterioration during the following days and consequently give rise to a higher risk of LND if they are not excluded.

In a newly published meta-analysis,<sup>27</sup> it was concluded that admission haematoma volume and IVH were associated with END; however, it was not shown that haematoma expansion was significantly related to END. Our study supports the notion that haematoma expansion is one of the key driving forces behind END. This study, as well as other studies, has found that patients with early predictors of haematoma expansion such as large haematoma,<sup>28</sup> anticoagulation treatment and spot sign<sup>3 19</sup> were more likely to undergo END. In addition, a few studies have shown a direct link between haematoma expansion and END.<sup>10 11 29</sup> In this study, we found the spot sign to be an important predictor of END. The spot sign is a well-recognised predictor of early haematoma expansion. It is likely that much of the effect of other predictors of END (larger haematomas and anticoagulation therapy) is mediated at least in part by the spot sign. This was also observed in this study, as some of the predictors of END lost predictive effect when the spot sign was considered in the model. This makes prediction of early neurological stability perhaps the most clinically useful utility of acute CTA, and spot sign assessment in patients with ICH should be recommended in all patients with acute ICH.

The consensus that patients with IVH are in risk of END seems to be well established.<sup>27</sup> Our data further

support Sun *et al*<sup>6</sup> in the link between LND and IVH. It is most likely that part of the process of both END and LND is driven by obstruction of the cerebrovascular fluid circulation and other harmful processes related to IVH.<sup>7 30 31</sup> We encountered two phenomena not described in great detail in the literature—delayed IVH and expansion of the IVH volume. Both of these have previously been described as independent predictors of poor outcome—to the best of our knowledge never before in relation to ND,<sup>32 33</sup> though intuitively correlated. Our study indicates that the final IVH volume is predictive of LND. This emphasises the need for follow-up imaging in all patients with ICH allowing earlier intervention.

It is clear from our results that the first week constitutes the primary critical period regarding functional outcome and long-term mortality. Even after we controlled for other well-known predictors of mortality and poor outcome<sup>26</sup> as well as surgical treatment strategies, ND remained an important independent predictor of functional outcome and mortality. As the stability of the patients during the first week is very critical, when it comes to functional outcome and mortality, this study emphasises the importance of targeting the underlying processes that drive the deterioration—haematoma expansion, obstruction of circulation in the fluid-filled spaces, and comorbidities. It is our belief that this study possesses excellent external validity. The trend today is towards a more fast track workup of patients with stroke due to the documented benefit of recanalisation therapies in ischaemic stroke. This entails that more and more patients with ICH also will be diagnosed early. We believe that our fairly unselected population and the few patients lost to follow-up makes our study a trustworthy picture of ND in patients with acute ICH.

## CONCLUSION

The first week constitutes a very critical period with a relative high incidence of ND. Stability during the first week entails a good prognosis. END seems to be directly associated with haematoma expansion. Obstruction of the fluid-filled spaces seems to be associated with both END and LND. Patients with a higher degree of comorbidity are at a higher risk of LND.

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